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10/596,062	06/20/2007	Yang Liu	22727/04398	1364

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CALFEE HALTER & GRISWOLD, LLP
800 SUPERIOR AVENUE
SUITE 1400
CLEVELAND, OH 44114

EXAMINER	
MYERS, CARLA J	
ART UNIT	PAPER NUMBER
1634	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

ipdocket@calfee.com
dcunin@calfee.com

Office Action Summary	Application No.	Applicant(s)	
	10/596,062	LIU ET AL.	
	Examiner	Art Unit	
	Carla Myers	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2009 and 29 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18* is/are pending in the application.

4a) Of the above claim(s) *1-6 and 8-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 May 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2/26/08 and 5/31/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group III, claim 7 in the reply filed on May 7, 2009 is acknowledged. The traversal is on the ground(s) that the technical feature linking the claims is not CD24 itself, but rather polymorphic forms of CD24. Applicants assert that the polymorphic forms of CD24 share the common activity of resulting in an increased likelihood that the subject will develop multiple sclerosis (MS).

This is not found persuasive because each polymorphism present in the CD24 gene does not share the common functional activity of being correlated with MS. For example, the findings in the specification indicate that the 1678A/G mutation is not correlated with MS (see page 39). Further, the post-filing date art of Goris (Journal of Neuroimmunology. 2006. 175: 200-202) teaches that the CD24 Val/Ala mutation is not correlated with risk of MS subjects from Belgium and the UK (see page 201, col. 2). Most importantly, each of the polymorphisms of CD24 do not share a common structure and activity essential to that structure, as is required to show that they are of the same nature since each of the recited polymorphisms differs from one another with respect to their nucleotide identity and their location. Additionally, it is maintained that the technical feature that links the claims (in the absence of both a common activity and a common structure) is the CD24 gene and its association with MS. However, an association between CD24 and MS was known in the art at the time the invention was made, and is specifically disclosed by Bai et al (Journal of Clinical Investigation. 2000. 105: 1227-1232; cited in the IDS). In particular, Bai teaches that deletion of CD24 (also referred to

as HAS) and the absence of expression of CD24 is correlated with experimental autoimmune encephalomyelitis, which is a model for human multiple sclerosis (page 1231). Thus, there is no special technical feature linking the recited groups, as would be necessary to fulfill the requirement for unity of invention.

Applicants further assert that the International Search Authority found that unity of invention was present in WO 2005/054810, from which the present application was filed as a National Stage Application, and thereby the claims possess unity of invention. However, the absence of a lack of unity requirement in a PCT application does not preclude a finding of a lack of unity at the National Stage of an application.

The requirement is still deemed proper and is therefore made FINAL.

2. Claim 7 has been examined herein.

Claims 1-6 and 8-18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on May 7, 2009.

Sequence Listing

3. The CRF and paper copies of the Sequence Listing filed on June 29, 2009 have been entered.

However, upon further review, it has been determined that his application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821-25 because the

previously submitted Sequence Listing does not include each of the sequences set forth in the present application. See, for example, para [087], and [089] of the specification and Figure 1. As these sequence disclosures are not pertinent to the claimed invention and in the interest of compact prosecution, this case has been examined on the merits. However, in response to this Office action, Applicants must comply with the requirements of 37 CFR 1.821-1.825. In particular, Applicant is required to submit a new CRF and paper copy of the Sequence Listing containing the additional sequence, an amendment directing the entry of the Sequence Listing into the specification, an amendment directing the insertion of the SEQ ID NOs into the appropriate pages of the specification and a letter stating that the content of the paper and computer readable copies are the same. Note that for those sequences appearing in Figure 1, a new Figure should be provided which includes the appropriate SEQ ID NOs for the recited sequences or the Brief Description of the Drawings should be amended to refer to the appropriate SEQ ID NOs recited in the figure.

Specification

4. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code – see, for example, para [062]. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Claim Rejections - 35 USC § 112 second paragraph

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 7 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 7 is indefinite over the recitation of "corresponds to SEQ ID NO: 1." Corresponding is not an art recognized term to describe the relationship between two nucleic acid sequences. It is not clear as to whether a corresponding sequence is intended to include only a sequence that is the same as the CD24 gene of SEQ ID NO: 1 or also includes a sequence that is similar to the CD24 gene of SEQ ID NO: 1 in that it contains any number of nucleotide deletions or deletions, and/or also includes a homologue or ortholog or isoform or splice variant of CD24, etc. Because the term "corresponds" has not been clearly defined in the specification and because there is no art recognized definition for this term as it relates to nucleic acid sequences, one of skill in the art cannot determine the meets and bounds of the claimed subject matter.

Claim 7 is also indefinite over the recitation of "which sequence" because this phrase lacks proper antecedent basis. While the claim previously refers to a nucleic acid sample and to a CD24 gene, the claim does not previously refer to a sequence. Also, it is unclear as to the relationship between the CD24 gene and the nucleic acid sample. That is, while the claim recites a step of obtaining a nucleic acid sample, the claim more broadly recites determining if there is a deletion of nucleotides 1580 and 1581 in a CD24 gene. The claim does not indicate the relevance of the step of obtaining the nucleic acid sample since the claim does not require that the CD24 gene that is analyzed for a deletion is present in the nucleic acid sample. Thereby, it is unclear as to how the step of obtaining a nucleic acid sample relates to the remainder of the claim.

Claim Rejections - 35 USC § 112 first paragraph - Enablement

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The following factors have been considered in formulating this rejection (*In re Wands,* 858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988): the breadth of the claims, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, the amount of direction or guidance presented, the presence or absence of working examples of the invention and the quantity of experimentation necessary.

Breadth of the Claims:

Claim 7 is drawn to a method for predicting the likelihood that an individual who has been diagnosed with multiple sclerosis (MS) will experience rapid progress of MS comprising determining if there is a deletion at positions 1580 and 1581 of the CD24 gene in the individual which sequence corresponds to SEQ ID NO: 1, wherein deletions of TG at positions 1580 and 1581 indicate that the individual has a greater likelihood of

experiencing rapid progression of MS than an individual diagnosed with MS and having TG at those positions.

Claim 7 broadly encompasses the analysis of any individual and thereby encompass the analysis of non-human individuals, include such diverse species as monkeys, dogs, rats, etc.

Claim 7 also defines the deletion in terms of occurring at positions 1580 and 1581 of the native CD24 gene "which sequence corresponds to SEQ ID NO: 1." The specification and prior art do not provide a clear definition for what constitutes "native CD24." Further, the term "corresponds" is not an art recognized term to define the relationship between two nucleic acids and the specification does not provide a clear definition for this term as it relates to nucleic acids. Accordingly, the term "corresponds" has been given its broadest reasonable interpretation as including sequences which are homologues or orthologues or isoforms or splice variants of SEQ ID NO: 1, or which are distinct in structure and function from SEQ ID NO: 1 but are by some unspecified means related to SEQ ID NO: 1. It is noted that the human genome includes at least 3 CD24 homologues located on chromosomes 6, 15, and Y (see Goris et al 2006, page 201). Since the location of the deletion is defined broadly in terms of a native CD24 gene which corresponds to SEQ ID NO: 1, the claims encompass the detection of a significant number of deletions in homologues, orthologues, splice variants, isoforms, and other mutants of the CD24 gene of any organism.

Nature of the Invention

The claims encompass methods for predicting the likelihood that an individual who has been diagnosed with MS will experience rapid progress of MS by assaying for a deletion at positions 1580 and 1581 of the CD24 gene. The invention is in a class of inventions which the CAFC has characterized as 'the unpredictable arts such as chemistry and biology" (Mycolgen Plant Sci., Inc. v. Monsanto Co., 243 F.3d 1316, 1330 (Federal Circuit 2001)).

Teachings in the Specification and State of the Art:

The specification teaches the occurrence of a deletion of nucleotides T/G at positions 1580 and 1581, relative to present SEQ ID NO: 1. The deletion occurs in the 3' untranslated region of the CD24 gene (page 38).

The specification provides the results of a genotyping study of the CD24 gene in 8 normal human subjects. As set forth in Table 2 (page 38), a deletion of nucleotides T and G at positions 1580 and 1581, relative to present SEQ ID NO: 1, appears to have been detected in at least one allele of 3 of the normal subjects.

The specification also provides the results of a genotyping study of the CD24 gene in 241 control and 221 MS patients. The genotyping study screened for the following polymorphisms: 226C/T, 1110A/G, 1580 and 1581 TG deletion, and 1678A/G (page 39). The specification reports that the 1110G allele showed the strongest association with MS and that the significance of the other SNPs requires further testing (see para [0109] and Table 3).

The specification also provides the results of a study to screen for a correlation between the 1580/1581 dinucleotide deletion and survival analysis (Example 7, page 40). The results are presented in Figure 6. Therein, the proportion surviving versus survival time in years is provided relative to individuals with the deletion at both alleles. The figure includes the annotation that: TG/TG vs. TG/del p=0.016, TG/TG vs del/del p=0.059, and TG/del vs del/del p=0.177. Since a p value greater than 0.05 is generally not considered to be statistically significant, Figure 6 appears to indicate only that individuals heterozygous for the deletion as compared to subjects homozygous for alleles lacking the deletion are correlated with longer survival. The specification does not provide any explanation as to why individuals heterozygous for the 1580-1581 deletion show a correlation with survival, whereas individuals homozygous for the 1580-1581 deletion do not show a correlation with survival, and individuals homozygous for the allele without a deletion also do not show a correlation with survival.

It is noted that the present claim recites that an individual having a deletion of TG at positions 1580 and 1581 has a greater likelihood of experiencing rapid progression of MS than an individual having TG at positions 1580 and 1581. It is also noted that the specification (para [010]) states that "As used herein in reference to MS, the term "rapid progression" means that an individual has reached or will reach EDSS 6.0 in a shorter time period than average from the time of first diagnosis of MS." However, the data provided in the specification appears to be limited to survival time and not to the time period that occurred before an individual reaches EDSS 6.0.

Further, in the post-filing date reference of Wang et al (The Journal of Immunology. 2007. 178: 129.1), of which the present inventors are co-authors, it appears that conflicting results were reported. Wang teaches that in a study of 316 MS patients and 342 controls, the 1580-1581 dinucleotide deletion was associated with significantly reduced risk of MS and delayed progression of MS.

Similarly, in the reference of Wang et al (PLoS Genetics. April 2007. 3: e49, 0508-0517), of which the present inventors are also co-authors, it is reported that the 1580-1581 dinucleotide deletion (referred to therein as $P1527^{del}$) is preferentially transmitted to unaffected individuals (page 0513, col. 2). Wang also teaches the results of a study that compared the proportion of survivors and years from first symptom for subjects having the del/del, del/GT and GT/GT genotypes (Figure 3 and page 0511). Wang reported that MS patients with the TG/del or del/del genotype had a more delayed disease progression as compared to MS patients with the TG/TG genotype.

On the other hand, Gonzalez (Neurology. March 2009. 72 (supplement 3), A376, abstract P08.040) studied the association between the CD24 1580-1581 dinucleotide deletion (referred to therein as the P1527 TG/del polymorphism) and protection against MS in a population from Argentina. Gonzalez found that there was no difference between the frequency of the mutation in subjects with MS as compared to controls and concluded that the deletion did not provide a protective effect against MS in the study population from Argentina.

The Predictability or Unpredictability of the Art :

The art of determining an association between a genotype and a phenotype, such as progression of MS, are highly unpredictable. Knowledge that the polymorphism is present in a subject having a phenotype does not permit one to predictably determine whether that polymorphism will be reproducibly associated with the phenotype. In particular, in the present situation, the information presented in the specification is not sufficient to permit one to ascertain whether deletion of nucleotides 1580 and 1581 in one or both CD24 alleles is correlated with rapid progression of MS. The data provided in the specification is not in fact directed to the study of the rate of progression of MS. Rather, the results presented in the present specification are limited to the analysis of survival time of patients with MS. Further, the results in Figure 6 are not statistically significant for the comparison of individuals homozygous for the deletion versus homozygous for the absence of the deletion ($p = 0.059$) or for individuals homozygous for the deletion versus individuals having one allele with the GT ($p=0.177$). Also, the conclusion provided in the present claims appears to conflict with the teachings of the present inventors in their post filing date reference in that claim 7 requires that a deletion of TG at positions 1580-1581 is correlated with increased likelihood of rapid progression of MS, whereas the Wang et al references cited above teach that a deletion of TG at positions 1580-1581 is correlated with a more delayed progression of MS.

Further, as discussed above, the claims broadly encompass the detection of a deletion of nucleotides 1580-1581 in a significantly large genus of genes that include paralogs, orthologs, isoforms, splice variants, mutant/deletion variants of CD24 and related genes, in human and non-human individuals. However, it is highly unpredictable

as to which if any of the broadly claimed deletions would be correlated with increased likelihood of experiencing rapid progression of MS.

The art is replete with evidence that gene association studies are frequently wrong. In fact, Lucentini et al (The Scientist (2004) Vol 18, page 20) titled his article "Gene Association Studies Typically Wrong" and teaches therein that reproducible association studies are "few and far between." The reference reports that "when a finding is first published linking a given gene with a complex disease, there is only roughly a one third chance that studies will reliably confirm the finding. When they do, they usually find the link is weaker than initially estimated. The first finding is usually 'spurious, or it is true, but it happens to be really exaggerated, ' ...there may be no way to predict which new gene-association studies will be verified with multiple replication." This is consistent with the teaching of Wacholder et al (J. Natl. Cancer Institute (2004) 96(6):434-442) who notes that "Too many reports of associations between genetic variants and common cancer sites and other complex diseases are false positives (see abstract). Ioannidis et al. (Nature genetics (2001) 29:306-309) further supports this conclusion in pointing out the heterogeneity of results among different studies of genetic polymorphisms (see abstract, for example).

The teachings in the specification support the unpredictability in the art in determining an association between a polymorphism in the CD24 gene and a phenotype, such as MS. In particular, the specification teaches that the CD24 1678A/G mutation was not correlated with MS (see page 39).

The post-filing date art also supports the unpredictability in the art of determining an association between CD24 polymorphisms and MS. Specifically, Goris (2006) teaches the results of a study of the frequency of the CD24 Ala/Val polymorphism in 1180 MS patients and 1168 controls from Belgium and the UK. Goris states that "We did not observe the previously reported overrepresentation of the T/T ($CD24^{V/V}$) genotype among MS patients in either of the study populations, nor in combined analysis. Indeed, there was a trend in the opposite direction, with an under-representation of the T allele in cases, in the UK population" (pages 201-202). Goris also did not find an association between this polymorphism and MS disease progression (page 202).

The unpredictability of extrapolating the results obtained from one organism (humans) to other organisms is emphasized by the teachings of Halushka (Nature. July 1999. 22: 239-247). Halushka studied the frequency of polymorphisms among different ethnic populations and between human and apes. The reference (see abstract, page 244 col. 2 and page 245, col 1) found that there was considerable diversity in the number and frequency of SNPs between different ethnic groups and between humans and orthologous great ape sequences.

Amount of Direction or Guidance Provided by the Specification and Degree of Experimentation:

The specification does not provide sufficient guidance as to how to apply the findings obtained therein to other deletions of nucleotides 1580-1581 in paralogs, orthologs, isoforms, splice variants, and other deletion and mutant variants of the CD24

gene. The specification does not exemplify the 1580-1581 deletion in a representative number of other CD24 genes and related sequences, other than in the sequence of present SEQ ID NO: 1.

In view of the unpredictability in the art and the lack of specific guidance provided in the specification, extensive experimentation would be required to practice the invention as it is broadly claimed. Such experimentation would require, for example, determining if there is a deletion of nucleotides 1580-1581 in the coding region or 5' untranslated region, or the intron sequences of native CD24 sequences, as will be variable depending on the numbering system employed for the gene (e.g., if the numbering begins at the first nucleotide of the fist codon, the first nucleotide known for the 5' untranslated region, the first nucleotide of the first intron etc). If such a deletion is identified, the experimentation would require determining if the deletion is present in subjects with rapid progression of MS and in subjects with delayed progression of MS, and then trying to ascertain if there is a statistically significant correlation between the deletion and rapid progression of MS. Additional experimentation would involve performing similar studies to analyze the other two human homologues of the CD24 gene, and other known orthologs or isoforms of the CD24 gene. The results of performing such experiments are highly unpredictable and thereby such experimentation is considered to be undue.

Further, the claims encompass methods which predict increased likelihood of rapid progression of MS in non-human individuals. However, the specification does not provide sufficient guidance as to how to predictably determine if the 1580-1581 deletion

is correlated with rapid progression of MS in a representative number of non-human individuals. The specification does not teach the occurrence of a 1580-1581 deletion in the CD24 gene of a representative number of non-human organisms or an association between this deletion and rapid progression of MS in a representative number of non-human organisms. In view of the lack of a clear structure-function relationship between the 1580-1581 CD24 deletion and rapid progression of MS and in view of the lack of specific guidance provided in the specification, undue experimentation would be required to practice the claimed invention in a representative number of non-human organisms.

Conclusions:

Case law has established that '(t)o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'" *In re Wright* 990 F.2d 1557, 1561. *In re Fisher,* 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) it was determined that '(t)he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art". The amount of guidance needed to enable the invention is related to the amount of knowledge in the art as well as the predictability in the art. Furthermore, the Court in *Genetech Inc. v Novo Nordisk* 42 USPQ2d 1001 held that '(I)t is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of the invention in order to constitute adequate enablement".

In the instant case, as discussed above, there is a high level of unpredictability in the art of determining an association between polymorphisms in the CD24 gene and rapid progression of MS. For the reasons set forth above, the teachings in the specification do not appear to establish the correlation required by the present claims that the presence of a deletion of nucleotides 1580-1581 (with respect to SEQ ID NO: 1) in one or both alleles of the CD24 gene is associated with increased likelihood of rapid progression of MS as compared to subjects having at least one TG at nucleotides 1580-1581 of the CD24 gene. Further, the findings in the present inventors post-filing date art appear to conflict with the requirements of present claim 7 in that the Wang et al references (The Journal of Immunology and PLoS Genetics) teach that MS subjects having a deletion of nucleotides 1580-1581 at one or both alleles are more likely to have a reduced progression of MS, as compared to MS subjects lacking a deletion of nucleotides 1580-1581.

Additionally, the specification does not provide guidance to overcome art recognized problems in the association of polymorphism with a phenotype, as shown by Lucentini, Wacholder, Ioannidis, and Halushka, among others. Further, the quantity of experimentation is significant. Additionally, the claims are significantly broad in scope in that they encompass methods which predict the likelihood of rapid progression of MS in any non-human subject, whereas the information provided in the present specification is limited to human subjects. Also, the claims include detecting a deletion of nucleotides 1580-1581 in a significantly large genus of genes, that may be homologues, orthologs, isoforms, splice variants, or other deletion or mutant variants of CD24 and related

genes, whereas the specification discloses only a deletion of nucleotides 1580-1581 in the fragment of the CD24 gene consisting of SEQ ID NO: 1. Accordingly, in view of the breadth of the claims, the unpredictability in the art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, and the negative teachings in the art balanced only against the high skill level in the art, undue experimentation would be required to practice the claimed invention.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carla Myers whose telephone number is 571-272-0747. The examiner can normally be reached on Monday-Thursday (6:30-5:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James (Doug) Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Carla Myers/

Primary Examiner, Art Unit 1634